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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/048,046	HALAZONETIS ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5,6,21,23 and 43-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5,6,21,23 and 43-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/01/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 1, 4, 7-20, 22, 24-42, and adds new claims 43-59, which are related to claims 2-3, 5-6, 21, 23 and are not new matter.

Accordingly, claims 2-3, 5-6, 21, 23, 43-59 are examined in the instant application.

The following are the remaining rejections.

OBJECTION

Claims 21, 23, 43-48 are objected to, for the use of the language "a nucleic acid sequence of 12 to 30 nucleic acids in length that is identical to SEQ ID NO:1" in claim 21.

It is noted that SEQ ID NO:1 is a full length sequence, of 2679 nucleotides, and thus it is not clear how a sequence consisting of only 12 to 30 nucleotides in length is identical to the full length sequence of SEQ ID NO:1.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claims 47-48, 57-58 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of detecting the sensitivity of tumor cells to an "anti-mitotic" drug claimed in Claims 47-48, 57-58 has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for detecting the sensitivity of tumor cells to an agent that disrupts microtubule function (p.5, line 4; p.27, lines 12-13, 16-17). There is however no mention of an "anti-mitotic" drug.

The subject matter claimed in claims broadens the scope of the invention as originally disclosed in the specification.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

1. Claims 47-48, 57-58 are indefinite for the use of the language "sensitivity" to an anti-mitotic drug in claims 47, 57. It is not clear what type of sensitivity is referred to. Does Applicant means sensitivity to killing by an anti-mitotic drug?

For the purpose of compact prosecution it is assumed that Applicant means sensitivity to killing by an anti-mitotic drug.

2. Claim 50 is indefinite for the use of the language "substantial absence".

The term "substantial" in claim 50 is a relative term which renders the claim indefinite. The term "substantial" is not defined by the claim, the specification does not

provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

3. Claims 48, 58 are indefinite for the use of the trademark "Taxol" in the claims.

MPEP 7.35.01 teaches that where a trademark or trade name is used, the claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name See *Ex parte Simpson*, 218 USPQ 1020 (Bd.App.1982). In the present case the trade name is used to describe and, accordingly, the description is indefinite.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 2-3, 5-6, 21, 23 are rejected under 112, first paragraph, pertaining to lack of a clear written description for reasons already of record in paper of 06/04/04.

New claims 43-59 are rejected for the same reasons already of record.

Applicant argues that claims are fully supported in the specification, which teaches sequences 12-30 nucleotides in length, that are complementary or identical to SEQ ID NO:1 or selected portions of SEQ ID NO:1. Applicant argues that these sequences are useful for detecting the expression of the wild type or mutated chfr gene.

Applicant argues that one would be able to prepare sequences complementary to SEQ ID NO:1 and fragments thereof without undue experimentation.

Applicant's arguments in paper of 11/01/04 have been considered but are found not to be persuasive for the following reasons:

It is noted that a complement to SEQ ID NO:1 or fragment thereof encompasses partial or full length complement wherein a partial complement would be complementary to SEQ ID NO:1 or fragments thereof by only a few nucleotides. Thus a sequence complementary to SEQ ID NO:1 or fragments thereof encompasses sequences with unknown structure which are complementary to SEQ ID NO:1 or fragments thereof via only a few nucleotides.

Further, a fragment of SEQ ID NO:1 that is complementary and binds to "chfr" encompasses a fragment of SEQ ID NO:1 that is complementary to and binds to variants of SEQ ID NO:1, the structure of which variants are not described in the specification, nor known in the art. Similarly the language "chfr" gene alone, as recited in claims 21, 47, 49, 50, without specifying that said "chfr" gene comprises SEQ ID NO:1, encompasses variants of SEQ ID NO:1, the structure of which is not disclosed.

In addition, a reagent or a kit for detecting a "mutation" of chfr gene , as claimed in claims 21, 23, 43-58, encompasses a reagent for detecting numerous variants of SEQ ID NO:1 having unknown mutation(s). Said mutation could be deletion, addition at any nucleotide position throughout the whole length of the sequence, or a substitution at any nucleotide position with any nucleotides, without any limitation of the number of nucleotides to be deleted, added, or substituted.

There is however no teaching in the specification concerning which mutation is to be detected by the claimed reagent or kit.

Further, the disclosed detected mutation at the non-coding strand, responsible for changing Val580 to Met580 in the C-terminal cysteine rich region of the encoded chfr (p.39, first paragraph), and a recombinant mutant having deletion of residues 2-142 encompassing the FHA domain (p.41, second paragraph) would not be a representative number of species of the genus of detected mutations, because the claimed detected mutation could be deletion, addition at any nucleotide position throughout the whole length of the sequence, or a substitution at any nucleotide position with any nucleotides, without any limitation of the number of nucleotides to be deleted, added, or substituted.

Moreover, the language "an isolated sequence which is an antisense sequence" of a sequence encoding at least amino acids 31 to 103, and/or amino acids 303 to 346 and/or amino acids 476 to 641 of new claim 59 is interpreted as open language "comprising" and thus the claim encompasses sequences with unknown structure of any length, that contains a few antisense nucleotides of the encoding sequence.

Thus the specification does not meet the written description requirement. The example of Lilly is clearly applicable to the instant application, because no representative number of species of the claimed complements, variants or antisense sequences, or detected mutations is disclosed, or known in the art, and no common structure among the claimed sequences is disclosed, or known in the art.

Further, the specification does not meet the written description requirement in view of the example of Enzo, because the specification does not disclose of sufficiently detailed, "relevant identifying characteristics, functional characteristics when coupled

with a known or disclosed correlation between function and structure, or some combination of such characteristics."

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Claims 2-3, 5-6, 21, 23 are rejected under 112, first paragraph, because while enabled for the polynucleotide of SEQ ID NO:1, the specification lacks enablement for a complement of SEQ ID NO:1 or fragments thereof, a variant of SEQ ID NO:1, a method for detecting a mutation of chfr gene, and a sequence which "is" an antisense sequence of a sequence encoding a fragment of SEQ ID NO:2, for reasons already of record in paper of 06/04/04.

New claims 43-59 are rejected for the same reasons already of record.

Applicant argues that one would be easily able to prepare the sequence of claim 2 and fragments thereof in new claims 44-46 and 59.

It is noted that a complement to SEQ ID NO:1 or fragment thereof encompasses partial or full length complement wherein a partial complement would be complementary to SEQ ID NO:1 or fragments thereof by only a few nucleotides. Thus a sequence complementary to SEQ ID NO:1 or fragments thereof encompasses sequences with unknown structure which are complementary to SEQ ID NO:1 or fragments thereof via only a few nucleotides.

Further, a fragment of SEQ ID NO:1 that is complementary and binds to "chfr" encompasses a fragment of SEQ ID NO:1 that is complementary to and binds to numerous variants of SEQ ID NO:1, the structure of which variants are not described in

the specification, nor known in the art. Similarly the language "chfr" gene alone, as recited in claims 21, 47, 49, 50, without specifying that said "chfr" gene comprises SEQ ID NO:1, encompasses numerous variants of SEQ ID NO:1, the structure of which is not disclosed.

Moreover, the language "an isolated sequence which is an antisense sequence" of a sequence encoding at least amino acids 31 to 103, and/or amino acids 303 to 346 and/or amino acids 476 to 641 of new claim 59 is interpreted as open language "comprising" and thus the claim encompasses sequences with unknown structure of any length, that contains a few antisense nucleotides of said encoding sequence.

Applicant has not taught how to make such complement or variants, or antisense sequences.

Applicant argues that one is able to determine if the chfr gene is expressed or if the gene is mutated, using the primers disclosed in the specification.

This is not found to be persuasive. A reagent or a kit for detecting a "mutation" of chfr gene , as claimed in claims 21, 23, 43-58, encompasses a reagent for detecting variants of SEQ ID NO:1 having numerous unknown mutation(s). The claimed detected mutation could be deletion, addition at any nucleotide position throughout the whole length of the sequence, or a substitution at any nucleotide position with any nucleotides, without any limitation of the number of nucleotides to be deleted, added, or substituted.

There is however no teaching in the specification concerning which of the numerous mutation(s) is to be detected, other than the disclosed detected mutation at the non-coding strand, responsible for changing Val580 to Met580 in the C-terminal

cysteine rich region of the encoded chfr (p.39, first paragraph), and a recombinant mutant having deletion of residues 2-142 encompassing the FHA domain (p.41, second paragraph).

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

1. If Applicant could overcome the above 112, first paragraph, new claims 47-48, and 57-58 are still rejected under 112, first paragraph, because while being enabled for a kit, useful for detecting the sensitivity to killing of cancer cells by nocodazole or Taxol, wherein detection of "lack the mRNA expression" of SEQ ID NO:1 is indicative of said sensitivity, the specification lacks of enablement for a kit, useful for detecting the sensitivity of tumor cells to an anti-mitotic drug, wherein detection of "the expression" of chfr gene is indicative of said sensitivity.

New claims 47-48, 57-58 are drawn to a reagent or a kit which is useful in a PCR assay for detecting the sensitivity of tumor cells to an anti-mitotic drug, wherein detection of "the expression" of chfr gene is indicative of said sensitivity.

The specification discloses that cells that express chfr survive better when exposed to nocodazole or Taxol, whereas cells that do not express detectable chfr are more sensitive to such agent (Example 4, especially pages 44-45, check).

Applicant recites the reference by Mariatos et al, stating that inactivating mutations in the chfr gene occur in cancer cells, and such inactivation correlates to higher sensitivity to anti-mitotic drug.

The recitation of Mariatos et al is acknowledged and entered.

It is noted that **detection of the expression of chfr gene in tumor cells encompasses detection of an "increase" or a "decrease" in the level of mRNA or an "unchanged presence" of mRNA of SEQ ID NO:1 as compared to normal control cells**.

It is not clear from the claims which expression is indicative of sensitivity to anti-mitotic drug.

Further, It seems however that only an absence of the mRNA of SEQ ID NO:1 is indicative of increased susceptibility to cell killing by the drug nocodazole or Taxol, as shown by Example 4 in the specification. There is no indication that tumor cells that express an increased or an unchanged level of mRNA of SEQ ID NO:1 as compared to normal control cells are sensitive to treatment with an anti-mitotic drug.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

2. If Applicant could overcome the above 112, first paragraph, new claim 50 is still rejected under 112, first paragraph, because while being enabled for a kit which analyzes the absence of the mRNA of SEQ ID NO:1, **the specification lacks enablement for a kit which analyzes cells for the "substantial absence of a chfr gene" or a combination of the "substantial absence of a a chfr gene" and a mutation of the chfr gene.**

New claim 50 is drawn to a kit which analyzes cells for the "substantial absence of a chfr gene" or a combination of the "substantial absence of a a chfr gene" and a mutation of the chfr gene.

It is noted that a "substantial absence of a chfr gene" encompasses reduction in the number of genomic copies of chfr gene, such as loss of an allele or loss of heterozygocity.

The specification only discloses a decrease in the mRNA level of SEQ ID NO:1. There is no indication that there exists a reduction in the number of genomic copies of the chfr gene comprising SEQ ID NO:1, such as loss of an allele or loss of heterozygocity, because mutational event is unpredictable.

Further, there is no correlation between a decrease in the mRNA level of SEQ ID NO:1 and a reduction in the number of genomic copies, because a change in the mRNA level could be as well due to change at the transcriptional level or to an increase in degradation of the mRNAs.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USC 102(b)

The amended Claim 2 is rejected under 35 USC 102(b) as being anticipated by Boehringer Mannheim Biochemicals, of record.

New claim 59 is rejected under 35 USC 102(b) as being anticipated by Boehringer Mannheim Biochemicals, for reasons already of record in paper of 06/04/04.

Claim 2 is drawn to a sequence "complementary" to SEQ ID NO:1.

Claim 59 is drawn to an "antisense sequence" of a sequence encoding at least amino acids 31-103, and/or 303-346, and/or 476-641 of SEQ ID NO:1.

Applicant argues that the primers of Boehringer are only 6 nucleotides in length, and thus Boehringer does not teach or suggest the 2679 nucleobase nucleic acid sequence of claim 2.

Applicant's arguments in paper of 11/01/04 have been considered but are found not to be persuasive for the following reasons:

Given the sequences taught by Boehringer one could readily envision the claimed complement or antisense sequence, because a complement or an antisense could be of any size, as long it contains a few complementary or antisense nucleotides.

REJECTION UNDER 35 USC 102(b), NEW REJECTION

1. Claims 21, 47-48 are rejected under 35 USC 102(b) as being anticipated by JP06303997-A, 1994, GenBank Accession No:AAQ75652.

Claim 21 is drawn to a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells, said reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1. Claims 47-48 are drawn to the reagent of claim 21, which is useful in a PCR assay to detect the sensitivity of tumor cells to an anti-mitotic drug, wherein said anti-mitotic drug is the Taxol agent.

Claims 21, 47-48 recite the claimed nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1, as a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells, or useful in a PCR assay to detect the sensitivity of tumor cells to an anti-mitotic

drug. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims 21, 47-48 read on the ingredient *per se*, which is a reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1.

It is noted that in view of a lack of a definition of a reagent in the specification, a reagent could be any compound, such as the primer recited in the cited art below.

JP06303997-A teaches a sequence of 21 nucleotides in length which is 100% similar to 21 nucleotides of SEQ ID NO:1, from nucleotide 2658 to nucleotide 2678, as shown by MPSRCH sequence similarity search (MPSRCH search report, 2005, us-10-048-046-1.oligo.rng, page 2).

The sequence taught by JP06303997-A seems to be the same as the claimed reagent.

In addition, in view the sequence taught by JP06303997-A one could readily envision the claimed complementary sequence.

2. Claims 21, 44 are rejected under 35 USC 102(e) as being anticipated by US 5,610054-A, GenBank Accession No:I57653.

Claim 21 is drawn to a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells, said reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is complementary to SEQ ID NO:1.

Claim 44 is drawn to the reagent of claim 21, which is complementary to the portion of SEQ ID NO:1 that encodes amino acids 31-103 of SEQ ID NO:2.

Claims 21, 44 recite the claimed nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1, as a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims 21, 44 read on the ingredient *per se*, which is a reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1.

It is noted that in view of a lack of a definition of a reagent in the specification, a reagent could be any compound, such as the primer recited in the cited art below.

It is further noted that nucleotides 81-399 of SEQ ID NO:1 encode amino acids 476-641 of SEQ ID NO:2, which is renumbered as 1-319 in MPSRCH search report.

US 5,610054-A teaches a sequence of 15 nucleotides in length which is 100% similar to 13 nucleotides of SEQ ID NO:1, from nucleotide 129 to nucleotide 141, as shown by MPSRCH sequence similarity search (MPSRCH search report, 2005, us-10-048-046-1.copy 81-399.oligo.rge, page 6).

In view of the sequence taught by US 5,610054-A, one could readily envision the claimed complementary sequence.

3. Claims 21, 45 are rejected under 35 USC 102(b) as being anticipated by Gold, DP et al, 1993, GenBank Accession No:S86452.

Claim 21 is drawn to a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells, said reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is complementary to SEQ ID NO:1.

Claim 45 is drawn to the reagent of claim 21, which is complementary to the portion of SEQ ID NO:1 that encodes amino acids 303-346 of SEQ ID NO:2.

Claims 21, 45 recite the claimed nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1, as a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims 21, 45 read on the ingredient *per se*, which is a reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1.

It is noted that in view of a lack of a definition of a reagent in the specification, a reagent could be any compound, such as the primer recited in the cited art below.

It is further noted that nucleotides 997-1128 of SEQ ID NO:1 encode amino acids 303-346 of SEQ ID NO:2, renumbered as 1-132 in MPSRCH search report.

Gold et al teach a sequence of 30 nucleotides in length which is 100% similar to 14 nucleotides of SEQ ID NO:1, from nucleotide 98 to nucleotide 111, as shown by MPSRCH sequence similarity search (MPSRCH search report, 2005, us-10-048-046-1.copy 997-1128.oligo.rge, pages 3-4).

In view of the sequence taught by George et al, one could readily envision the claimed complementary sequence.

4. Claims 21, 46 are rejected under 35 USC 102(b) as being anticipated by George JF et al, 1992, GenBank Accession No:S81367.

Claim 21 is drawn to a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells, said reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is complementary to SEQ ID NO:1.

Claim 46 is drawn to the reagent of claim 21, which is complementary to the portion of SEQ ID NO:1 that encodes amino acids 476-641 of SEQ ID NO:2.

Claims 21, 46 recite the claimed nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1, as a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims 21, 46 read on the ingredient *per se*, which is a reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is identical or complementary to SEQ ID NO:1.

It is noted that in view of a lack of a definition of a reagent in the specification, a reagent could be any compound, such as the primer recited in the cited art below.

It is further noted that nucleotides 1516-2013 of SEQ ID NO:1 encode amino acids 476-641 of SEQ ID NO:2, wherein said nucleotides are renumbered as 1-498 in the MPSRCH search..

George JF et al teach a sequence of 27 nucleotides in length which is 100% similar to 14 nucleotides of SEQ ID NO:1, from nucleotide 138 to nucleotide 151, as shown by MPSRCH sequence similarity search (MPSRCH search report, 2005, us-10-048-046-1.copy 1516-2013.oligo.rge, pages 1, 4-5).

In view of the sequence taught by George et al, one could readily envision the claimed complementary sequence.

REJECTION UNDER 35 USC 103 (a), NEW REJECTION

1. Claim 3 is rejected under 35 USC 103(a) as being anticipated over Boehringer Mannheim Biochemicals, of record, in view of Sambrook et al, 1989, 2nd ed, Molecular cloning, A laboratory manual, Cold Spring Harbor laboratory Press, Cold Hpring Harbor, p.10.13.

Claim 3 is drawn to a sequence "complementary" to SEQ ID NO:1, which is synthetically or recombinantly produced.

Boehringer Mannheim Biochemicals teaches a kit comprising random primers that encompass all possible 6-nucleotide sequences (see page 93, Catalog No. 1034 731/1006 924).

Boehringer Mannheim Biochemicals does not teach that the primers are synthetically or recombinantly produced.

Sambrook et al teach that random primers can be obtained by three ways: 1) digesting calf thymus or salmon sperm DNA, 2) purchasing random oligonucleotides from commercial sources, such as Boehringer Mannheim, or 3) synthesizing on an automated DNA synthesizer.

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to make the primers taught by Boehringer Mannheim Biochemicals synthetically or recombinantly to produce a large quantities of primers for commercial purpose, without the cost of buying them commercially. One of ordinary skill in the art would have been motivated to make the primers taught by Boehringer Mannheim Biochemicals synthetically or recombinantly with a reasonably expectation of success.

2. Claims 23, 43, 49-58 are rejected under 35 USC 103(a) as being obvious over JP06303997-A, supra, in view of US 5,324,630.

Claim 23, 43 are drawn to a reagent useful for detecting the expression of the wild-type chfr gene or a mutation of said gene in cells, said reagent consisting of a nucleic acid sequence of between 12 to 30 nucleic acids in length, that is complementary to SEQ ID NO:1, wherein said reagent further comprising a detectable label, which could be a fluorescent label or an enzyme.

Claims 49-58 are drawn to:

a) A kit for detecting expression of the wild type chfr gene and/or a mutation of said chfr gene in a cells, said kit comprising at least one component selected from the group consisting of (i) a fragment of SEQ ID NO:1 that is between 12 to 30 nucleotides

in length, that is complementary and binds to chfr, and ii) a fragment of SEQ ID NO:1 that is between 12 to 30 nucleic acids in length (claims 49-50),

b) The kit of claim 49,wherein the nucleotide fragment is attached to a detectable label, which could be a fluorescent compound or an enzyme (claims 51-52).

c) The kit of claim 49 further comprising one or more components that detect said labels, or instructions for performing said kit, microtiter plates to which the nucleic acid sequences have been pre-adsorbed, diluents, buffers, applicator sticks, containers, or sample preparator cups (claims 53-54),

d) The kit of claim 49,wherein the nucleotide fragment is synthetically or recombinantly produced (claim 55),

e) The kit of claim 49, further comprising instructions for performing PCR (claim 56). Said kit of claim 49 is useful in a PCR assay to detect the sensitivity of tumor cells to an anti-mitotic drug, wherein detection the expression of the chfr gene or a mutation of said chfr gene is indicative of said sensitivity (claim 57). Said antimitotic drug is the Taxol agent.

The teaching of JP06303997-A has been set forth above. JP06303997-A further teaches analysis of cDNA and gene expression, by amplification.

JP06303997-A does not teach a detectable label, which could be a fluorescent label or an enzyme. JP06303997-A does not teach a kit, comprising PCR instructions, or comprising a component that detects the labels, or instructions for performing said kit, microtiter plates to which the nucleic acid sequences have been pre-adsorbed, diluents, buffers, applicator sticks, containers, and sample preparator cups.

JP06303997-A does not teach that the nucleotide fragment is synthetically or recombinantly produced.

US 5,324,630 teaches a diagnostic kit comprising a labeled nucleic acid probe in a container, and instruction for the detection method (claim 3). US 5,324,630 teaches that suitable labels could be enzymes, fluorescers (column 8, llines 13-16). US 5,324,630 teaches that polymerase chain reaction technique may be used for the production of the probe and/or amplification of the polynucleotides for synthetic purpose (column 4, lines 28-31). US 5,324,630 teaches that synthetic or natural DNA fragment could be used (column 4, lines 37-38).

It would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to label the sequence with suitable labels such as enzymes, fluorescers taught by US 5,324,630, for use in the diagnosis of gene expression as taught by JP06303997-A.It would have been obvious to formulate the sequence taught by JP06303997-A in a kit, which contains instructions for detection methods, as taught by US 5,324,630, wherein said detection method could be a polymerase chain reaction, as taught by US 5,324,630, for commercial purpose. It would have been obvious to make the sequence taught by JP06303997-A synthetically or recombinantly by PCR as taught by US 5,324,630, because these methods would produce an abundant amount of DNA fragments.

One of ordinary skill in the art would have been motivated to label the sequence taught by JP06303997-A, and formulate in a diagnostic kit taught by US 5,324,630 with a reasonable expectation of success.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

February 03, 2005

SUSAN UNGAR, PH.D
PRIMARY EXAMINER